APPENDIX A

Applicants: Stephen E. Lincoln and
                      Michael R. Knapp
Serial No.:   09/618,178
Filed: 18 July 2000

Clean Copy of Amended Claims

51.   (Amended)   A method according to claim 72, wherein the reaction values are measurements of an optical signal or a digital image intensity value.

52.   (Amended)   A method according to claim 74, wherein the reaction values are measurements of an optical signal or a digital image intensity value.

56.   (Amended)   A method according to claim 72, wherein the reaction values are obtained by assaying for alleles using a method selected from the group consisting of genetic bit analysis, hybridization, allele-specific amplification and a ligase chain reaction.

58.   (Amended)   A method according to claim 74, wherein the reaction values are obtained by assaying for alleles using a method selected from the group consisting of genetic bit analysis, hybridization, allele-specific amplification and a ligase chain reaction.

60.   (Amended)   A method according to claim 72, further comprising detecting the presence of a downward trend in confidence scores over time.

62.   (Amended)   A method according to claim 72, wherein the reaction values are obtained by assaying for one or more alleles that provide information relating to a trait.

63.   (Amended)   A method according to claim 74, wherein the reaction values are obtained by assaying for one or more alleles that provide information relating to a trait.

64. (Amended)   A method according to claim 72, wherein one or more of the reaction values are obtained by assaying for one or more alleles that provide information pertaining to parentage of the subject.

65. (Amended)   A method according to claim 74, wherein one or more of the reaction values are obtained by assaying for one or more alleles that provide information pertaining to parentage of the subject.

66. (Amended)   A method according to claim 72, wherein more than one genetic loci are analyzed.

67. (Amended)   A method according to claim 72, wherein the reaction values are obtained by assaying for one or more alleles that provide information useful for determining the identity of the subject.

68. (Amended)   A method according to claim 74, wherein the reaction values are obtained by assaying for one or more alleles that provide information useful for determining the identity of the subject.

C.   establishing a distribution set of probability distributions, including at least one distribution, associating hypothetical reaction values with corresponding probabilities for each genotype of interest at the locus;

D.   applying the first reaction value to each pertinent probability distribution to determine a measure of a conditional probability of each genotype of interest at the locus; and

E.   determining the genotype based on the data obtained from step (D).

76.   (New) A method according to claim 75, wherein the distribution set includes a plurality of probability distributions for a corresponding plurality of genotypes of interest.

77.   (New) A method, according to claim 75, further comprising:

(i)   reacting the material at the locus to produce a second reaction value independently indicative of the presence of a second allele at the locus;

(ii)   forming a second data set including the second reaction value; and

(iii) applying the first and second reaction values to each pertinent distribution to determine a measure of the conditional probability of each genotype at the locus.

29302.1

78.   (New) A method according to claim 76, further comprising:

    (i)   reacting the material at the locus to produce a second reaction value;

    (ii)   applying the first and second reaction values to each pertinent distribution to determine the probability of each genotype at the locus; and

    (iii)   applying the first and second reaction values to each pertinent distribution to determine a measure of the conditional probability of each genotype at the locus.

D'
cout.

79.   (New) A method according to claim 77, wherein each probability distribution associates a hypothetical pair of first and second reaction values with a single probability of each genotype of interest.

80.   (New) A method according to claim 75, wherein:

step (B) includes the step of including in the data set other reaction values obtained under conditions comparable to those under which the first reaction value was produced; and

step (C) includes the step of using the reaction values in the data set to establish the probability distributions;

the method further comprising:

performing steps (D) and (E) with respect to each of the reaction values.

81.   (New) A method, according to claim 80, of determining the genotype at a locus within genetic material obtained from each of a plurality of samples, the method further comprising:

(i)   performing step (A) with respect to the locus of material obtained from each sample;

(ii)   in step (B), including in the data set reaction values obtained from each sample.

82.   (New) A method according to claim 80, of determining the genotype of selected loci within genetic material obtained from a sample, the method further comprising:

(i)   performing step (A) at each of the selected loci;

(ii)   in step (B), including in the data set reaction values obtained from each of the selected loci.

83.   (New) A method according to claim 80, wherein step (C) includes:

(i)   establishing a set of initial probability distributions that associate hypothetical reaction values with corresponding probabilities for each genotype of interest at the locus;

(ii)   using the initial probability distributions to determine measures of the initial conditional probability for each genotype at the locus; and

(iii)   using the results of step (ii) to modify the initial probability distributions, so that the modified distributions more accurately reflect the reaction values in the data set.

84.   (New) A method according to claim 83, wherein step (C) further includes:

(iv) repeating steps (i) through (iii) a desired number of times.

85.   (New) A method according to claim 75, wherein step (E) further includes the step of calculating a confidence score, associated with the genotype being determined, based on data obtained from step (D).

86.   (New) A method according to claim 80, wherein step (E) further includes the step of calculating a confidence score, associated with the genotype being determined, based on data from step (D), the method further comprising:

29302.1

(F) determining whether a significant downward trend in confidence scores has occurred, and, in such event, entering an alarm condition.

87.   (New) A method according to claim 75, wherein each allele is a single specific nucleotide.

88.   (New) A method according to claim 75, wherein each allele consists of at least two specific nucleotides.

89.   (New) A method according to claim 75, wherein each allele is defined at least in part by its length in nucleotides.

90.   (New) A method according to claim 75, wherein each allele is defined by one of the presence and absence of at least one restriction site.

91.   (New) A method according to claim 78, wherein step (B) includes the step of including in the data set reaction values from prior tests at the locus obtained under comparable conditions.

92.   (New) A method according to claim 82, wherein the loci are selected on the basis of their ability to discriminate among subjects.

93.   (New) A method, according to claim 77, wherein the step A' of reacting the material involves using a different reaction from that of step A and the second allele is different from the given allele.

94.   (New) A method according to claim 75, wherein step (A) includes the step of assaying for the given allele using genetic bit analysis, allele-specific amplification, polymerase chain reaction, or a ligase chain reaction.

95.   (New) A method according to claim 82, wherein the loci are proximal to one another, so that the set of genotypes so produced may indicate a sequence of nucleotides associated with the genetic material. - -

REMARKS

A. Summary of the Invention

Broadly, the subject invention concerns a method for determining the genotype at a genetic locus for a sample of genetic material obtained from a biological sample. The method includes a step of reacting the material at the locus to produce a first reaction value indicative of the presence of a given allele at the locus. A data set is formed which includes at least the first reaction value. The method of the invention also includes a step of establishing a distribution set

29302.1